

Application No. 10/082,036  
Confirmation No. 9501  
Attorney's Docket No. 09367.0019-01000

### REMARKS

It is respectfully requested that this application be reconsidered in view of the above amendments and the following remarks and that all of the claims remaining in this application be allowed. Claims 24-34 and 36-45 are pending. Claims 39-42 and 44-45 have been withdrawn from consideration, but should be examined upon allowance of a relevant generic claim.

Claims 24 and 31 have been amended to specify that a phenotypic fingerprint comprises a group of scalar or vector descriptors wherein said descriptors characterize morphological or compositional features of a cell. See, for example, paragraphs 7, 9 and 93. To expedite prosecution, Applicants have amended claims 24 and 31 to recite this definition explicitly. Applicants respectfully maintain that no new matter has been added by the amendment.

#### *Rejections under 35 U.S.C. §102(b)*

##### Hofland et al.

Claims 24-34 and 36-38 stand rejected under 35 U.S.C. §102(b), as allegedly being anticipated by Hofland et al. These rejections are respectfully traversed.

Hofland et al. discloses a method for co-culturing human breast-cancer cells with tumor-derived fibroblasts. Various growth factors were added to the two cells and the resulting cell proliferation rate measured. In all experiments, only a single quantitative measure was obtained, the number of tumor cells or fibroblasts. Furthermore, this value was not generated from an image. Cell numbers were obtained by measuring DNA content using bisbenzimidazole fluorescent dye (p. 94, left column) or by measuring <sup>3</sup>H-thymidine incorporation (p. 95, right column). Thymidine incorporation was measured by scintillation counting of an entire vial (p. 94, left column). DNA content was reported on a per well basis (Fig. 2), with no spatial information given.

Figure 3 of Hofland et al. contains double-stained images showing both BUdR incorporation and keratin staining. However, no quantitative measures were generated from these images. Instead, the images served as qualitative gauges of the proliferating cell type. Keratin staining (red-brown) is simply an on-off measure that distinguishes epithelial tumor cells (on) from fibroblasts (off). BUdR (blue) staining indicates newly grown cells. From the double-

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staining experiments, the authors confirmed that the proliferating cells were mainly epithelial cells, permitting them to interpret the  $^3\text{H}$ -thymidine incorporation results as representing the proliferation of epithelial cells (p. 95, left column).

Thus Hofland et al. obtains qualitative indicators from an image, and obtains a single quantitative measure from a non-imaging experiment. Hofland et al. does not disclose a method including quantitatively evaluating an image to generate a phenotypic fingerprint comprising a group of scalar or vector descriptors wherein said descriptors characterize morphological or compositional features of a cell, as recited in amended claims 24 and 31. As such, Hofland et al. cannot anticipate independent claims 24 and 31 and their dependent claims 25-30, 32-34, and 36-38. Applicants respectfully request withdrawal of these rejections.

Stearns et al.

Claims 24-29, 31-34, and 36-38 stand rejected under 35 U.S.C. §102(b), as allegedly being anticipated by Stearns et al. These rejections are respectfully traversed.

Stearns et al. discloses a method for studying the effect of prostate cancer cells on microvessel formation by bone marrow endothelial cells in the presence of various reagents. Average microvessel length was measured in a defined area of a light microscopy image (Tables 1 and 2, Figs. 1 and 7). Separately, ELISAs were performed to measure TIMP-1 and MMP-2 secretion by different cell types. ELISA measurements represent absorbance at 490 nm for an entire experiment. They provide no spatial information and do not yield or require images. The microvessel results in Tables 1 and 2 and Figs. 1 and 7 represent different experiments from the ELISA measurements of Figs. 2-6.

Thus Stearns et al. obtains a single quantitative measure from an image, and additional quantitative values from different non-imaging experiments. Stearns et al. does not disclose a method including quantitatively evaluating an image to generate a phenotypic fingerprint comprising a group of scalar or vector descriptors wherein said descriptors characterize morphological or compositional features of a cell, as recited in amended claims 24 and 31. As such, Stearns et al. cannot anticipate claims 24 and 31 and their dependent claims 25-29, 32-34, and 36-38. Applicants respectfully request withdrawal of these rejections.

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Zietlow et al.

Claims 24-34, 36-38, and 43 stand rejected under 35 U.S.C. §102(b), as allegedly being anticipated by Zietlow et al. These rejections are respectfully traversed.

Zietlow et al. discloses a method for evaluating the effect of activated microglia on the survival of dopaminergic neurons. Cell survival was ascertained by counting the number of tyrosine hydroxylase-positive cells in a defined area or volume (p. 1659, left column). Although the shape and size of some cells were noted (p. 1659, right column), the only quantitative measurement obtained was cell number. In other experiments, the effect of neuronal- or astrocyte-conditioned medium on microglial expression of iNOS was measured (p. 1659, right column). All microglia were stained with OX42, and microglia expressing iNOS were stained with anti-iNOS. In the double-staining experiments, however, cell combinations alone were studied, and not the effect of an agent on the cells. The activating agents, FMLP and Zymosan A, were not included in the iNOS expression studies.

Thus the method of Zietlow et al. generates only a single quantitative value from an image of cells exposed to an agent. Zietlow et al., therefore, does not disclose a method including quantitatively evaluating an image to generate a phenotypic fingerprint comprising a group of scalar or vector descriptors wherein said descriptors characterize morphological or compositional features of a cell, as recited in amended claims 24 and 31. As such, Zietlow et al. cannot anticipate independent claims 24 and 31 and their dependent claims 25-30, 32-34, 36-38, and 43. Applicants respectfully request withdrawal of these rejections.

None of the prior art references, either alone or in combination, suggests or teaches the generation of phenotypic fingerprints as recited in claims 24-34 and 36-45. These phenotypic fingerprints provide advantages in automation and scalability, among many other advantages, that the prior art references lack.

In view of the above, Applicants submit that this application is now in condition for allowance. A notice to that effect is earnestly solicited.


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If it is determined that a telephone conversation would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

Respectfully submitted,

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Dated: September 1, 2004

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